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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
HENRY, MICHAEL C

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 07/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,465	PETIT ET AL.	
	Examiner	Art Unit	
	Michael C. Henry	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P ri d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23,24 and 32-40* is/are allowed.

6)☒ Claim(s) *1-22 and 25-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-40 are pending in application

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statement filed complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4,6-9,13-17,20,21 are rejected under 35 U.S.C. 102(b) as being anticipated by Falk et al. (US 5,985,850).

In claim 1, applicant claims " a method for increasing the transport of a biologically active agent into mammalian cells comprising: contacting the cells with a medicament comprising the agent and at least one carbohydrate, so that the carbohydrate enhances the absorption of the agent into the cells relative to the absorption of the agent in the medicament lacking carbohydrate." Falk et al. disclose a method for increasing the transport of a biologically active agent (lasix, furosemide) into mammalian cells (intraveneously) comprising: contacting

the cells with a medicament comprising the agent (furosemide) and at least one carbohydrate (hyaluronic acid), so that the carbohydrate (hyaluronic acid) enhances the absorption of the agent (furosemide) into the cells relative to the absorption of the agent (furosemide) in the medicament lacking carbohydrate (hyaluronic acid) (col. 32, CASE XXIX, lines 37-45). Falk et al. disclose that "hyaluronic acid increases penetration/permeation of the drug and thus facilitates its function (col. 32, lines 43-45). Claim 2 is drawn to the method of claim 1 wherein the agent and carbohydrate are in an aqueous vehicle. Claim 2 is anticipated by Falk et al., since Falk et al. agent and carbohydrate are in water (see col. 17, lines 40-47 and col. 18, lines 8-10). Claim 3 is drawn to the method of claim 2 wherein the medicament is a solution, suspension, or gel. Claim 3 is anticipated by Falk et al., since Falk et al. administers his composition intravenously which implies the use of a solution (col. 32, CASE XXIX, lines 37-45). In claim 6, applicant claims a method of claim 1 wherein the weight ratio of carbohydrate: agent is about 4:1-15:1 in aqueous solution, either after preparation with aqueous solvent or after delivery into the aqueous environment surrounding the cells. Falk et al. disclose applicant's method of claim 6 wherein weight ratio of carbohydrate: agent is 15:1 (300 mg hyaluronic acid: 20 mg of furosemide) in aqueous solution after preparation with aqueous solvent (col. 32, CASE XXIX, lines 37-45). It should be noted that since Falk et al. medicament contains water, then the agent (furosemide) and the carbohydrate are in an aqueous solution. In claim 7, applicant claims a method of claim 1 wherein the weight ratio of carbohydrate: agent is at least 7:1 in aqueous solution, either after preparation with aqueous solvent or after delivery into the aqueous environment surrounding the cells. Falk et al. disclose applicant's method of claim 7 wherein weight ratio of carbohydrate: agent is 15:1 (300 mg hyaluronic acid: 20 mg of furosemide) in aqueous solution after

preparation with aqueous solvent (col. 32, CASE XXIX, lines 37-45). It should be noted that since Falk et al. medicament contains water, then the agent (furosemide) and the carbohydrate are in an aqueous solution. In addition, throughout their specification, Falk et al. refer to the hyaluronic acid as a carrier/penetrating agent (which enhances or increases penetration or transport)(e.g., see col. 27, lines 34-44; col. 21, lines 52-55).

Claims 1,10 are rejected under 35 U.S.C. 102(b) as being anticipated by Falk et al. (US 5,792,753).

In claim 10, applicant claims the method of claim 1 wherein the cell is an epithelial cell. Falk et al. disclose applicant's method claim 10 wherein the cells are epithelial cells of the dermis (skin). Falk et al. topical application comprises diclofenac (Voltaren) in hyaluronic acid (sodium hyaluronate) (example 8, col. 36, lines 7-17).

Claims 22, 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Illum (US 5,744,166).

In claim 22, applicant claims a method of claim 1 wherein the agent is a peptide. Illum discloses a method for increasing the transport of a biologically active agent (insulin: a peptide hormone) into mammalian cells (intranasally) comprising: contacting the cells with a medicament comprising the agent (insulin) and at least one carbohydrate (chitosan: a polycationic carbohydrate), so that the carbohydrate (chitosan) enhances the absorption of the agent (insulin) into the cells relative to the absorption of the agent (insulin) in the medicament lacking carbohydrate (insulin) (example 4, col. 9, line 36 to col. 10, line 23). Illum discloses that polycationic polymer (such as chitosan) promote delivery of therapeutically effective amounts of the pharmacologically active agent to a mammal upon administration (col. 3, line 13-26). In

claim 25, applicant claims a method of claim 1 wherein the agent is a nucleotide or nucleic acid. Illum claims applicant's method of claim 25 wherein the agent is ribonucleic acid or deoxyribonucleic acid (see claim 19).

Claims 18, 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Flueren (WO 97/14310).

In claim 18, applicant claims the method of claim 14 wherein the carbohydrate comprises a sugar alcohol. In claim 19, applicant claims the method of claim 18 wherein the sugar alcohol comprises sorbitol ....." Flueren discloses applicant's method of claim 18 wherein the sugar alcohol comprises sorbitol and the active agent is a fungicidal agent, phytopthora infestans, and the absorption is into the cells on tomato plants (page 21, Table 5, lines 13-21).

Claims 27-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Schmidl (US 5,438,042).

In claim 27, applicant claims a dry composition comprising at least one carbohydrate and an amino acid, wherein the ratio of total carbohydrate to amino acid is about 1.5:1-20:1. Claim 28 is drawn to a composition of claim 27 wherein the amino acid is glutamine. Schmidl et al. disclose applicant's dry composition of claims 27 and 28 wherein 65 to 85% is carbohydrates and 14 to 30% by weight is glutamine (see abstract). This means that the total carbohydrate to amino acid is about 6:1 when the percent of carbohydrate to glutamine (amino acid) is 85% to 14%) (see abstract). It should be noted that Schmidl et al. composition can also be in solid powder form (dry form) or can be mixed with water (see col. 3, lines 37-40). Thus, claims 30

and 31 which are drawn to aqueous solutions of the composition of claim 29 are also anticipated by Schmidl et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1,4,5,8,11,12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Falk et al. (US 5,985,850).

In claim 5, applicant claims a method of claim 1 wherein the medicament is an aqueous solution comprising about 20-99 weight percent carbohydrate.

Falk et al. disclose a method wherein the medicament is an aqueous solution comprising about 300 mg hyaluronic acid: 20 mg of furosemide (col. 32, CASE XXIX, lines 37-45).

The difference between applicants' claimed method and the method of Falk et al. is that Falk et al. do not disclose the weight percent carbohydrate. However, the weight percent carbohydrate is a matter of choice that is dependent on factors like the quantity and type of the cells contacted with the medicament and age and weight of the individual containing said cells.

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have used the process of Falk et al., for increasing the transport of a biologically active agent into mammalian cells and, to use different concentrations and ratios of active agent to carbohydrate, depending on need.

One having ordinary skill in the art would have been motivated, to use the process of Falk et al., for increasing the transport of a biologically active agent into mammalian cells and, to use different concentrations and ratios of active agent to carbohydrate, depending on need. It should be noted that claims 11 and 12 which are drawn to specific cells (cells of gastrointestinal tract and endothelial cells) are also encompassed by this rejection, since Falk et al. disclose that hyaluronic acid enhances the penetration of several drugs into cells, in general, including drugs that are taken orally, like antibiotics (e.g.col.11, line 13).

Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (US 5,744,166).

In claim 26, applicant claims a method of claim 1 wherein the agent is a steroid.

Illum discloses a method for increasing the transport of a biologically active agent (insulin: a peptide hormone) into mammalian cells (intranasally) comprising: contacting the cells with a medicament comprising the agent (insulin) and at least one carbohydrate (chitosan: a polycationic carbohydrate), so that the carbohydrate (chitosan) enhances the absorption of the agent (insulin) into the cells relative to the absorption of the agent (insulin) in the medicament lacking carbohydrate (insulin) (example 4, col. 9, line 36 to col. 10, line 23). Illum discloses that polycationic polymer (such as chitosan) promote delivery of therapeutically effective amounts of the pharmacologically active agent to a mammal upon administration (col. 3, line 13-26). In addition, Illum discloses that steroidal anti-inflammatory agents can be used (col. 4, line 46 to col.5 line 8, especially col. 4, line 61).

The difference between applicants' claimed method and the method of Falk et al. is that Illum do not use a steroid. However, Illum discloses that a steroid can be used as an active agent.

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have used the process of Illum, for increasing the transport of a biologically active agent into mammalian cells, and to use a steroid as active agent, based on need, since Illum teach that a steroid can be used.

One having ordinary skill in the art would have been motivated, to use the process of Illum, for increasing the transport of a biologically active agent into mammalian cells, and to use a steroid as active agent, based on need, since Illum teach that a steroid can be used.

Claims 1,2,3,8,9,13-16,20,21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Culliford et al. (J Physiol. 1995 Dec. 15; 489 (Pt. 3): 755-65).

In claim 8, applicant claims a method of claim 1 wherein the medicament is a dry preparation and the weight ratio in the medicament of carbohydrate to agent is about 1.5:1-20:1. In claim 9, applicant claims the method of claim 8 wherein the agent is glutamine.

Culliford et al. disclose a method of significantly increasing the membrane transport of glutamine (an amino acid) by suspending red blood cells in isotonic sucrose (see abstract).

The difference between applicant's claimed method and the method of Culliford et al. is that Culliford et al. do not disclose the weight percent of carbohydrate: agent (glutamine) and the physical state of the carbohydrate and the agent in terms of dryness. However, the use of specific weight percent of carbohydrate: agent (glutamine) and, carbohydrate and agent (glutamine) of specific physical state (like dryness) is the is a matter of choice that is dependent

on factors like the quantity and type of the cells contacted with the medicament and age and weight of the individual containing said cells.

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have used the process of Culliford et al., for increasing the transport of a biologically active agent like glutamine into mammalian cells, and to use different concentrations and ratios of carbohydrate to active agent, depending on need.

One having ordinary skill in the art would have been motivated, to use the process of Culliford et al., for increasing the transport of a biologically active agent like glutamine into mammalian cells, and to use different concentrations and ratios of carbohydrate to active agent, depending on need.

Allowable subject Matter

The following is an examiner's statement of reasons for allowance: The examiner has found claims 23,24,32-40 to be unobvious over the prior art of record and therefore to be allowable over the prior art of record. The present invention relates to a process for increasing the transport of a biologically active agent into mammalian cells comprising: contacting the cells with a medicament comprising the agent (for example an amino acid) and at least one carbohydrate, so that the carbohydrate enhances the absorption of the agent into the cells relative to the absorption of the agent in the medicament lacking carbohydrate." The very relevant prior art document (US 5,985,850) to this invention discloses a process for increasing the transport of a biologically active agent into mammalian cells comprising by contacting the cells with a

medicament comprising an agent and at least one carbohydrate, so that the carbohydrate enhances the absorption of the agent into the cells relative to the absorption of the agent in the medicament lacking carbohydrate." However, though the process of the present invention is similar to that disclosed in the prior art document, they possess differences which includes active agents that are unobvious to those of the prior art, and that are not suggested or taught by the prior art document. More specifically, the process of the present invention does not utilize or suggest said method involving the use of amino acids as the active agent in combination with a carbohydrate to treat physiological disorders as disclosed in the prior art document.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 703 308-7307. The examiner can normally be reached on 8:30 am to 5:00 pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703 308-4624. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-1235.

MCH

July 22, 2003.

SAMUEL BARTS
PRIMARY EXAMINER
GROUP 1600